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A Record of the Progress of Pharmacy and the Allied Sciences

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CONTENTS

Editorial:
The Supreme Court and the Harrison Act 133
Bugs 135

Original Articles:
What Shall I Drink? By Horatio C. Wood, Philadelphia, Pa. 136
The Alkaloids of Ceanothus Americanus. (Illustrated.) By A. H. Clark, Chicago, Ill. 147
Application of Micro Methods to Control Work in Pharmaceutical Manufacturing. (Illustrated.) By Wm. Figdor, Bloomfield, N. J. 157
On the Instability of the Sodium Salt of Benzoylhydrogenperoxide. By Arnold J. Gelarie, New York City, and Frederick R. Greenbaum, Philadelphia, Pa. 163
Some Insects and Their Relation to Man. By M. A. Reasoner, Major, Medical Corps, U. S. Army 167
Scientific and Technical Abstracts 177
Book Reviews 189

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THE AMERICAN
JOURNAL OF PHARMACY

VOL. 98 MARCH, 1926 No. 3

EDITORIAL

THE SUPREME COURT AND THE HARRISON ACT

"EVERY MAN should know a little law," said Sir Edward Coke, and the author of "The Comic Blackstone," a humorous sketch that appeared in *Punch* many years ago, added, "the less the better." Few things irritate a lawyer more than for one not of his profession to presume to discuss the decisions of courts or the interpretation of legal documents. Yet even the courts of last resort (or as the scoffers sometimes call them courts of last guess), are but human and the frequent instance of division among the members of what is now probably the most famous court in the world, the U. S. Supreme Court, shows that even the best trained lawyers may fail to see subjects in the same light. Courts not infrequently incorporate in their decisions sentences which may be said to be rather the expression of feelings than direct opinions on the subject in hand. These, technically known as *obiter dicta,* "wayside speeches," may, however, be seriously meant, that is, information as to what the court might do if the subject before it was not exactly that upon which the decision is made.

The application of these remarks is to a recent utterance of the Supreme Court concerning the now somewhat popular method of controlling objectionable businesses by means of taxation. A prominent instance of such method is what is known as the Harrison Act, which regulates the sale and distribution of certain habit-forming drugs. It has been burdensome on both doctors and druggists, and it may be very seriously doubted if it has materially diminished the illicit practices. The statistics that have been published give but an incomplete view of the traffic, for they cannot account for the vast amount of secret trading that takes place. In this connection it may be noted that the legislation in restriction of the use of alcohol has

a markedly different relation to the public than is the case with drug restriction. Morphin, cocain and heroin have no industrial application. Their only use is for their specific physiologic effects. If morphin is taken to relieve suffering it is a legitimate use, whether one-eighth of a grain or more is used, but if taken to secure its peculiar effects by a person not suffering from pain it is an act of drug-addiction. Now, alcohol occupies an entirely different position. It has extensive industrial uses in which it is indispensable, hence a restriction of its manufacture in quantities sufficient for its special physiologic effects is absolutely out of the question. Not only is it used as alcohol in many ways, but it is converted into a very large number of substances which cannot be prepared from any other source. It is, therefore, possible to restrict the production of the ordinary habit-forming drugs to the amount necessary for their legitimate medicinal use but this cannot be thought of in the case of alcohol. It has been proposed, indeed, of late to limit the production of opium to the quantity necessary in the therapeutics.

Returning to the question of taxation, the Supreme Court has recently as is now generally known, held, in the Child Labor cases, that the action of Congress in trying to suppress child labor over the whole country by imposing a tax on the products of such labor passing from one state to another, is in violation of the Constitution. The court's opinion contains the sentence: "But there comes a time in the extension of the penalizing features of the so-called tax when it loses its character as such and becomes a mere penalty with the characteristic of regulation and punishment. Such is the case in the law before us." Inasmuch as the Harrison Act seems to be exactly of this character it is possible that if a case under it was brought before the court and argued by able attorneys a majority might hold that the act is not valid under the Constitution. In such a case the act, and all the machinery which has been put into operation under it, would collapse, and free traffic in habit-forming drugs be established. Whether this would make matters any worse cannot be said at present. Courts of last resort occasionally discover that they have made a mistake in a decision, in which case they either solemnly reverse themselves in a subsequent decision, or they so overlay the original decision with distinctions and exceptions that it is no longer of any use in jurisprudence. Public opinion may reach a point where the court may be compelled to change its attitude, but it does not seem that the general public in this country is as much aroused to the dan-

ger of the use of habit-forming drugs as it is to the danger in the use of alcohol. Certainly, no such general pressure has been brought to bear upon legislative bodies in restriction of the sale of morphin, cocain and heroin and similar substances, as has been brought in the case of intoxicating beverages. It is for instance not at all probable that such a movement as is embodied in the Harrison Act would find the support of a constitutional amendment which is back of the Volstead Act.

It is rash for one who is not a lawyer to point out what may be results of a court decision, but it is worth while to note that there is a Federal Act which has been many years in operation that applies this principle of taxation as a means of restriction. This is the "National Banking Act," passed under the stress of the War between the States, containing a provision by which banks other than national banks are subject to a tax of 10 per cent. on any notes that they may issue. There is no direct prohibition of any bank issuing notes, but it will be seen that the cost is prohibitory. There is a not inconsiderable minority in the country that believes in cheap money, and it may be that if a court holds that such taxation is unconstitutional there will be an opening for a state bank currency, the evils of which those of us are old enough to well remember.

After all it seems strange that the legislation in regard to drug-addiction should be allowed to go on with comparatively little public interest, while legislation in regard to alcohol is resented by all classes of society. The use of alcohol and tobacco are as much vices as the use of morphin, cocain, and heroin, but the former are gentlemen's vices (nowadays ladies' also) while the other indulgences are not considered respectable, yet physiologically they are in the same class.

HENRY LEFFMANN.

BUGS

ENTOMOLOGICALLY this word refers to any insect of the suborder Heteroptera. Etymologically it has a diversity of meanings. In the middle English and the Welsh, variants of it meant the goblin and the bogey-man. Later, it came to mean an insect of any sort, irrespective of zoologic classification. Still later, in the reckless mill of American slang it has acquired a brand new character. Thus

one who specializes in any field becomes a "Bug"—one who shows enthusiasm over pursuit or hobby or pastime is likewise labelled. There also is a most striking application of the word in our slang, when its pronouncement marks the dismissal of a subject with the most profound and final contempt.

Thus to the man in the street, the venerable member of the Fifth Estate, shortening his span of life seeking solution of the cross-word puzzle of God and the Universe, is a "Bug" and all who dabble in science are "Bugs."

To the slang-maker, who accepts his all, as dumbly "as a fish accepts the ocean"—every altruistic notion, every fine emotion—meets with the same grandeloquent comment—"Bugs!"

But we did not mean to elaborate so on the etymology of the word except perhaps that its zoologic and its slang interpretation both apply to the following context.

Enthusiasm is as dangerous as it is necessary. It affects vision, and its progenitors, though perchance developing a most acute sense for distance actually become blind to the near and the obvious.

And certainly it is fatal to lift the eyes to far horizons if in the meantime we omit to note the pitfalls and the inclines and the quicksands on the trail.

A Government publication on poisonous insecticides and fungicides inspired the foregoing remarks.

For certainly, in man's battle against the invading hordes of insects that come to devour his crops and his cattle-fodder, the enthusiasm of those who direct the plan of warfare, has somewhat dimmed the effectiveness of their tactics.

For just as the winds of the western front blew back to the German lines the venomous vapors they released to decimate the Allied ranks on that fateful day in history,—so will the reckless poisons broadcast by the "Bug" experts of State and Federal governments "blow back" to kill, not the beetle and caterpillar hosts, but the very humans whose existence they seek to protect.

Indeed, it is already happening—for with arsenic in our apples—and copper and arsenic in celery and salad and cabbage—and with the soil of our potato patches saturated with the vicious Paris green, enough of these atrocious poisons are used each season to constitute a serious menace to the welfare of the race.

Read the following announcement of a new insecticide and fungicide, which comes well recommended and agree with the writer

that the indiscriminate recommendation of such a compound, without extensive study as to its ultimate disposal in the plant, well qualifies the slang application of the term "Bug" to the one who proposes its widespread use:

"Consternation among the bug pests of Southern California is expected to follow the introduction of calcium cyanide, a new death-dealer which appears to be the most powerful agricultural poison yet known.

"Recent field tests show that calcium cyanide is much more potent than pure hydrocyanic acid, or prussic acid, heretofore considered the ultimate 100 per cent. of toxic power. This unexpected result so far is not explained. After one test of calcium cyanide this winter in an orange grove, where a very resistant strain of scale insects was infesting the foliage, only two bugs were found alive among over 3000 insects actually counted. This record is especially encouraging to growers who have found the scale pests gradually developing immunity to regular doses of hydrocyanic acid. As one orchardist suggests—'the ancestors of the scale have been killed so often that their progeny don't mind it any more.'

"Calcium cyanide, while theoretically appearing to be a simple preparation to the ordinary chemist, is impossible to make in any ordinary way. By combining calcium carbide with hydrocyanic acid, however, a light brown powder is secured, and this substance has the remarkable power of pouring out a veritable wave of poison gas when it is merely exposed to common air. Fumigators simply blow the poison in a dust cloud under the regular orchard tent; and whatever animal was living under the tent dies, regardless of whether it be a scale insect, a luckless owl or an itinerant rooster."

We might add that whatever animal, including the human, was living within a range of a mile of the fumigated region would suffer some from the cyaniding. And imagine placing so potent an instrument in the hands of the average "orchardist," then ask the question "What becomes of the cyanide?"

And what becomes of the millions of pounds of arsenic annually imported into America for insect destruction?

Why is it that the druggist almost makes a ceremony out of a sale of cyanide, while it and other potent poisons may be purchased *ad libitum* from a dealer in garden supplies?

Truly, so important a matter of public health calls for sane consideration which it is apparently not receiving at the hands of the enthusiasts responsible for compiling these special bulletins of State and Federal departments.

IVOR GRIFFITH.

ORIGINAL ARTICLES

WHAT SHALL I DRINK?*

Horatio C. Wood, M. D.

THE TENDENCY of man to mix "victuals with drink" seems to be almost a biologic instinct; from the earliest records of history in every land and clime, various races of peoples have sought to supplement their diet with some sort of beverage. The earliest records of ancient Babylon and Egypt show an acquaintance with wine; in Europe wine and beer were the popular drinks of early times; in Asia, tea, and in Northern Africa, coffee, have been used for many centuries. In Paraguay the Indians brewed a beverage they called "Maté" from the leaf of a tree that grows there; in Brazil the Guarani Indians made a drink from the seed of a native tree; in Florida the Indians prepared from the leaf of a species of holly, a beverage they called "Yaupon"; while the modern flapper tribe of North America are addicted to a drink they call "soda water."

Horatio C. Wood, M. D.

A custom so universal must be based upon some reason more potent than whim or tradition. At first thought it is difficult to see any unifying relation between substances of such diverse origin, different flavor and dissimilar effects. When we examine, however, more closely into the action of these beverages we find they have in common the power of alleviating the sense of fatigue, and I believe in this action we can find a sufficient explanation for their employment.

The important beverages may be divided into two great classes, those that contain alcohol and those that contain caffeine. The earliest alcoholic drinks were made by the fermentation of juices of fruits, especially of the grape. A little later man learned to prepare

*One of a series of popular lectures given at the Philadelphia College of Pharmacy and Science, 1925-1926 season.

from cereal grain such drinks as beer, ale, etc. The spirituous liquors, made by distillation of either wine or malt liquor, including brandy and whiskey, are comparatively recent introductions. While the effects of wine and beer are somewhat modified by the presence of sugars and artificially introduced flavoring, such as hops, nevertheless alcohol is the dominating principle; whether it be wine, whiskey or bootleg, the chief poisonous ingredient is alcohol. We read much in the newspapers today of deaths from drinking various illegal beverages, and there is a strong tendency to attribute these deaths to some unnatural ingredient. We forget that long before prohibition days the deaths from acute alcoholic poisoning far outnumbered those from bichloride of mercury, or opium, or carbolic acid or any other poison. Dr. Reid Hunt, of Harvard University, has recently shown that the most poisonous ingredient present in freshly distilled whiskey or "moonshine" is alcohol.

Alcoholic beverages are popularly referred to as "stimulants," but strictly speaking they are not stimulating. Alcohol is essentially a narcotic, similar in its general effects to ether or chloral. In the advanced stage of alcoholism the drinker lies flaccid, in a profound comatose sleep in which it is almost impossible to awaken the slightest evidence of consciousness, the skin covered with sweat, and the pulse soft and muscles flabby; no one would dream of regarding such a condition as an evidence of stimulation. There have been physiologists in the past, however, who, while admitting that large doses of alcohol are depressing, maintained that in small quantities the drug acts as a stimulant. In support of this view have been quoted such well-known facts as the increased fluency of the after-dinner speaker, the unusual courage of the timid man, or the geniality of the reticent. None of these, however, seem to me convincing evidence of exalted function. It is not the great talkers who are the best thinkers; nor is pugnacity a sign of strength.

When we come to actual scientific evidence we find an almost universal agreement among present investigators that alcohol in any dose sufficient to exert an effect, lessens intellectual efficiency. Space will not permit the recital of even a small part of the evidence upon this subject, most of which is reviewed in the standard textbooks on Pharmacology. I shall refer to only one interesting observation, that of Frankfurter, made in 1914. As a measure of efficiency, Frankfurter utilized, among other experiments, the amount of matter

which he could copy upon a typewriter within a given period of time. He found that under the influence of small amounts of alcohol, corresponding to one or two ounces of whiskey, there was a slight decrease in speed, amounting on an average to some 5 per cent., with an enormous decrease in accuracy; the number of mistakes he made was about double those that he made on the non-alcoholic days. A most interesting and characteristic observation was that while under the influence of the alcohol he had the feeling that he was working with extraordinary rapidity and efficiency, and it was only when he came to count the actual number of words that he had written, that he was able to free himself from erroneous conviction of a stimulating effect.

One of the earliest and most characteristic of the alterations in mentality, brought about by alcohol, is this lessening of the judgment faculty, the ability to estimate correctly one's capabilities and weaknesses. It is this loss of judgment which may beget foolhardiness in the ordinarily timid man, and develops in an automobilist that reckless willingness to take a chance, which makes the intoxicated driver such a menace to the community. I might call your attention in this connection to the fact that this is an early manifestation of alcoholism; a man is mentally incapacitated for proper management of an automobile long before there is any obvious evidence of intoxication, such as disturbance of equilibrium or loss of control of speech.

As to the effects of alcohol on muscular power, there is some room for difference of opinion. All experimenters are agreed that large quantities definitely diminish muscular strength; but there is considerable evidence that after small quantities, say half an ounce of absolute alcohol, there is a temporary increase in the contractile powers of the muscles. This increase seems to last but a few minutes and then be followed by a secondary depression which carries muscular power below the normal.

I have said that the reason for the use of beverages is to remove the sensation of fatigue. Some of you may be asking how this statement can be reconciled with the summary just given of the physiological effects of alcohol. Alcohol does not counteract fatigue, it does not refresh the system; it abolishes, or lessens, the unpleasant sensations of tire through its narcotic influences. It stupifies, not revives.

Tea

Next to wine, probably the oldest beverage is tea. When we talk of ancient civilizations there is likely to come to our mind pictures of Tut-Ankh-Amen lying in his golden sarcophagus, or the buried glories of Babylon and Damascus, forgetting that there is a civilization still extant, which was contemporaneous with that of ancient Egypt. More than a thousand years before the time of Tut-Ankh-Amen, there reigned in China an emporor by the name of Chen Nung. To Chen Nung may be accorded the credit of having originated the idea of a pharmacopœia. Four thousand years ago he had made by the royal physician, a collection of recipes and descriptions of the drugs which were used at that time; some of these are still official. To this famous ruler the Chinese also attribute the introduction of tea. Whether or not this tradition be correct, it is certain that the use of the beverage in Asia is of great antiquity. The famous philosopher and moralist of the Celestial Kingdom, Confucius, who lived in the Sixth Century, B. C., says in one of his aphorisms: "Be courteous to all even to the stranger from other lands; if he say unto thee that he thirsteth give him a cup of warm tea."

Although the use of tea spread early into Japan and Korea, it did not reach Europe until the Sixteenth Century. After its introduction into France and England it did not capture the popular fancy as rapidly as did coffee, which entered Europe about the same time. Perhaps the reason for the early lack of interest in tea was the price. During the Seventeenth Century the price of tea in England ranged around $5 a pound, which when we consider the comparative purchasing power of money of that day and this, would probably be equivalent to some forty or fifty dollars today.

After the East India Company turned their attention to the tea trade, however, the price of the leaf was brought down to a reasonable figure and the beverage became very popular in England. It was destined also to become a substance of great political importance. It was this Chinese leaf that became the precipitating cause of the political freedom of a people on the opposite side of this terrestrial globe. Old George III, with an obstinacy bordering on the insane, deaf to the advice of some of his statesmen, refused to recall the tea tax he had imposed on the western colonies, a tax which was of no financial importance to the mother country, but one of those matters of principle about which we have always been so pugnacious. The first

overt act of rebellion was the famous Tea Party in the Boston harbor.

The tea plant is a large shrub, a native of China; when left to itself it grows to the height sometimes of ten or fifteen feet, but under cultivation is usually trimmed to a bushy shape and not more than five or six feet tall. The methods of curing the leaf vary greatly in different parts of the world; each locality has its own tradition of the proper way of preparing the leaf. All of these methods fall into two groups, one of which produces "black" and the other "green" tea. In the production of black tea, the leaves are spread out in the sun for a few hours until they begin to wilt, then collected into bags and trampled upon to press out some of the sap; after this they are piled into heaps for varying periods of time, generally about a day, where they undergo a sort of fermentation. As a result of this fermentation they become dark in color and lose much of their tannic acid. After this they are thoroughly dried either in the sun or by artificial heat and shipped into commerce. In the process for green tea, the fermentation step is omitted; the fresh leaves, either with or without preliminary drying in the sun, are directly heated in a sort of a kiln with constant stirring until they reach a temperature too hot for the hands of the workers to endure. They are then removed and rubbed between the hands to give them a curled, twisted shape, and thoroughly dried.

Coffee

The most popular beverage of America is certainly coffee. Among drinks it is a comparatively modern habit, certainly not over 2000 years old. In Arabia, where the use of coffee originated, there are current many legends about how the drink came to be known; nearly all of these legends attribute its introduction to some follower of Mahomet, and as Mahomet lived in the Seventh Century, it would seem probable that the use of coffee is less than 1500 years old.

The first coffee house in Europe was established in Constantinople in 1554, and shortly afterwards similar places were established in Paris and London. So rapidly did coffee drinking take hold of the public taste that as early as 1675, Charles II of England felt called upon to forbid coffee houses as public nuisances because the frequenters were given to "seditious talk and slanderous attacks on persons of high position." Perhaps it is because of our inborn tendency to

indulge in slanderous attacks on persons in high positions, that has made us the greatest coffee drinkers on the face of the globe. Not only does the United States, as a nation, consume more coffee than England, Germany, France, Italy and Russia combined, but there is scarcely a single country, with the possible exception of Holland, where the per capita consumption is as great as in this land of liberty. The amount of coffee imported into the United States per annum, is equivalent to about ten pounds for every man, woman and child in the country.

The *Coffea arabica* is a small tree bearing some superficial resemblance to our common choke cherry, although not botanically allied to it. A native of northern Africa, it is now cultivated in many sub-tropical countries of the world. At present about 80 per cent. of the world's supply of coffee comes from Brazil; smaller quantities come from other South American countries, from Java and other of the East Indies. Very little real Arabian coffee enters the United States. In recent years a related species, *Coffea liberica,* has been experimented with and promises to become of commercial importance.

The fruit is a berry which may be either red or purplish, when ripe, and about the size of a small cherry, containing two seeds which are the parts used in preparing the beverage. The pulp of the fruit is separated from the seeds by means of large metal rollers provided with knobs. The seeds freed from the pulp are washed and allowed to soak in water in order to loosen the parchment membrane which still covers them. They are then dried and winnowed and ready to enter commerce as raw coffee.

The most important step in the preparation of coffee is the process of roasting. During this heating there is developed an empyreumatic oil, to which is due the characteristic flavor of the beverage, much of the water is evaporated and some of the tannin is destroyed. If the roasting be too severe or too long continued, some of the aromatic oil, at first formed, will volatilize, and the coffee acquire a bitter taste; there will also be lost some of the caffeine, to which it owes is physiological effects. If the bean be not sufficiently roasted it lacks in aroma and contains too much tannic acid. The tendency today is rather toward too little than too much roasting; there is a great loss of weight during he process of roasting, and as both raw and roasted coffee are bought and sold by the pound, it is obvious that there is a strong temptation not to cook the coffee too much.

After the roasting, the flavoring principle, being volatile, must disappear more or less rapidly unless the coffee be kept hermetically sealed. This loss of flavor takes places much more rapidly in ground coffee than when the bean is still whole. I am very much inclined to the opinion that the present day habit of buying coffee ready-ground has robbed many a cup of coffee of its proper aroma.

Maté, which has recently been introduced into this country, is a beverage that has been used for centuries by the Indians of Paraguay. It is made from the leaves of a species of holly, *Ilex Paraguayensis.* It is interesting to note in this connection that in Florida the Indians made a drink they called "Yaupon" from the *Ilex Vomitoria.* Guarana is another South American beverage made from the seed of the *Paullinia Cupana.* It is named for the tribe of Guarani Indians among whom it is popular. In this country it is used as a drug rather than a beverage.

All of these drinks, tea, coffee, maté, yaupon and Guarana, depend for their popularity chiefly upon the presence of the alkaloid caffeine. The ordinary cup of tea represents on the average about 1.5 grains of caffeine, a cup of coffee about 2.3 grains.

Effects of Caffeine

Caffeine is a true stimulant both to mental and muscular activity. The most extensive study of its effects upon mental processes is that of Professor Hollingsworth, at that time connected with Columbia University, which was made in 1912. During this study he had sixteen persons living under controlled conditions for a period of forty days, every day reporting to his psychological laboratory where they were put through all sorts of tests. On certain days they would be given caffeine in a capsule and on other days they would be given a capsule of similar appearance but containing starch instead of caffeine. Time will not permit me to describe in detail the various tests employed, in nearly all of which there was distinct evidence of the stimulating effect from caffeine lasting from two to eight hours. An interesting contrast to the effects of alcohol was shown in the typewriting test. Hollingsworth found that small doses of caffeine—less than three grains—produced a slight increase in the rapidity of typewriting, while large doses, five or six grains, produced some slowing of the work. The most striking result, however, was that either large

or small doses caused a marked diminution in the number of mistakes made, the decrease amounting to about 30 per cent. on the average.

Another important effect was brought out in the test was on mathematical calculation. In this the subjects were given a series of numbers to which seventeen was to be added, mentally, as rapidly as possible; the test of efficiency was the time required to do each series of problems correctly. As the day wore on the solutions became gradually slower, doubtless due to the effects of fatigue. If caffeine was given, about an hour after taking it there would be a marked increase in the rapidity with which the additions were performed; sometimes the problems would be done even more rapidly than at the beginning of the day. This stimulating effect would endure throughout the remainder of the day (about five hours).

Some years ago I undertook a study on the effects of caffeine upon muscular fatigue, entirely apart from any influence it might have upon the nerve centers. The method employed was to stimulate the muscle of a frog at short intervals with an electric current, until it became too exhausted to respond. In every instance the total amount of work done by the muscle which had previously been caffeinized was greater than that performed by a non-treated muscle from the same animal.

I think the opinion of Professor Rivers, although delivered in 1911, gives concisely the general consensus among pharmacologists today. He says: "The general practical conclusions to be drawn from the experiments I have recorded, and from those of previous workers, is that caffeine increases the capacity for both muscular and mental work, this stimulation persisting for a considerable time after the substance has been taken, without there being any evidence, after moderate dose, of reaction leading to diminished capacity for work; the substance thus really diminishing and not merely obscuring the effects of fatigue."

In closing, may I say a few words concerning the habitual use of caffeine beverages? In the first place, it cannot be denied that there is a possibility of injurious effects from this drug, but I think the dangers of the evils of caffeine addiction are greatly overestimated by a large proportion of the medical profession as well as of the laity. This popular notion of the harmfulness of tea and coffee is doubtless due, in large measure, to the persistent hammering

by the advertisers of certain substitutes. I do not believe that for the ordinary healthy adult, the habitual use of either coffee or tea in moderate quantities has any injurious effects.

There are certain individuals whose nervous systems are peculiarly sensitive to the effects of caffeine, in whom relatively small doses produce an undesirable excitation, and who should therefore avoid these drinks. We find these personal peculiar susceptibilities to many drugs and foods. There are some persons who cannot eat fish; there are other persons who cannot drink milk, but no one would care to deny the value of milk and fish as foodstuffs. There is another group of people with delicate stomachs whose digestion may be deranged by the other ingredients, especially the tannic acid, in tea and coffee.

Of course, any good thing can be abused. The late Sir William Osler, when living in the United States, remarked that more Americans suffered from overeating than from overdrinking (referring, of course, to alcoholic drinks); but the fact that many people injure themselves by eating, does not prove the habit a pernicious one. Any fool can injure his constitution by reckless over-indulgence in coffee, but it is a waste of breath to talk to fools.

There is one possible danger in the use of caffeinic drugs by the ordinarily sensible person and that is, that it enables a person to go beyond his normal limits of endurance, to expend some of his reserve energy. Caffeine is not a food, it does not restore power to exhausted nerve cells. The feeling of fatigue is the safety signal that nature has provided in order that we may know when we are drawing too heavily upon our reserve strength; caffeine delays the tinkling of the fatigue bell and encourages us to keep on without the proper amount of rest. It is like the man with money in his pocket; the mere fact that the money is handy tempts the spendthrift to throw it away, but the thoughtful man does not spend beyond his means simply because the money happens to be in his pocket. Caffeine does not injure the recuperative powers of the sensible, but it does tempt the health-spendthrift to lavish expenditures of energy. I believe that children, however, are much more prone to evil results from this stimulant effect. Not only are their nervous systems more sensitive to drug effects, but they are lacking in discretion in the matter of conservation of energy and are much more liable than adults to drive themselves to exhaustion.

THE ALKALOIDS OF CEANOTHUS AMERICANUS*

A. H. Clark

The Plant and Its Uses

CEANOTHUS AMERICANUS, Jersey tea, New Jersey tea, red shank, red root, Walpole tea, or wild snowball, is a shrub or bush growing very abundantly throughout the mountainous regions of eastern United States particularly in barren and dry woodlands. It is also found much less abundantly scattered over the central and western states on arid and sandy soil. It belongs to the Rhamnacea family and nearly all books on medicinal plants and any very complete botanical work give a description of it.

Its leaves have been used as a substitute for tea. Infusions of the entire plant or parts of it such as the leaves, flowers, seeds, root, or bark of the root have been used as an astringent in various ways this property usually being ascribed to the tannin which is present in the plant. Its use in connection with the treatment of syphilis, gonorrhœa, dysentery, asthma, bronchitis, whooping-cough, cancer, ulcerations of the mouth and throat and other diseases as well as a purgative have all been mentioned.

Present interest in the drug lies in a seemingly new discovery in connection with the therapeutics of it. Taylor and others (work yet unpublished) have recently shown that it has marked blood pressure reducing properties and is an active hemostatic when administered orally, very materially reducing the time of clotting of the blood. A careful search of the literature revealed but one reference to its use along these lines. Hammond in the *Georgia Eclectic Medical Journal,* Atlanta, 1879-80, 1, 355-359, states that "it is one of our very best remedies in passive uterine hemorrhage." He used a tincture of the root bark, four ounces to a pint of diluted alcohol and administered it in teaspoonful doses every hour "until its wonderful effects are manifest." Aside from the fact that some of the results reported from its use might be traced to a styptic action due

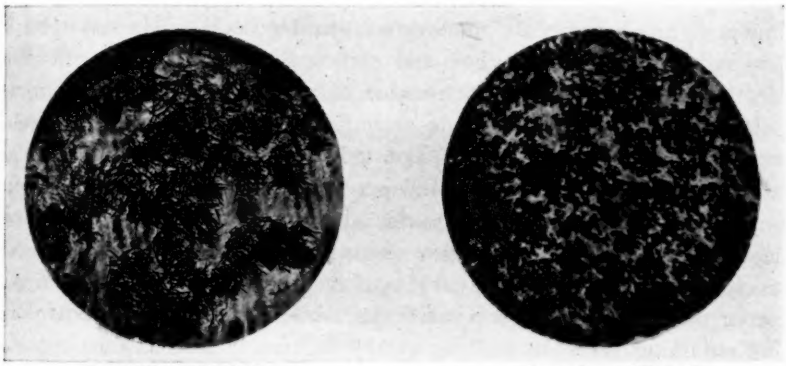
*This study was undertaken at the request of Mr. Guy C. Taylor, Chief Chemist of Flint, Eaton & Co., Decatur, Ill. It was begun in the University of Illinois School of Pharmacy and carried to the present point in the University of Michigan College of Pharmacy. Much of the crude alkaloid used in the beginning of the investigation was supplied by Mr. Taylor, and Flint, Eaton & Co. have provided an unlimited supply of crude drug and solid extract made from the drug.

to tannin there has been found but one reference to the use of Ceanothus americanus for this purpose. The *Boston Medical and Surgical Journal,* 1836, XV, p. 42, publishes a report in which it is stated that "a strong decoction of the bark of the root or the fresh root itself is a most valuable styptic for restraining hemorrhage from wounds." Even this action may have been due entirely to the tannin.

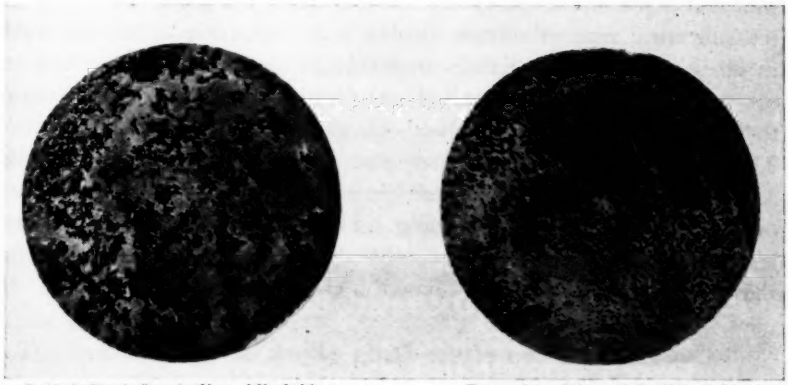
The present chemical study of the root bark was prompted by the discovery of the hemostatic and blood pressure reducing action and it is hoped to continue the work until some definite information is gained regarding the active constituents of the plant.

The Plant Constituents

Very little has been published regarding the constituents of Ceanothus americanus. King's *American Dispensatory,* 1859, p. 201, states that the leaves were said to contain tannin, a soft resin, bitter extractive, greenish coloring matter almost like green tea, gum, a volatile substance, lignin, and an active principle called *ceanothine.* This *ceanothine,* according to the *New York Journal of Organic and Medical Chemistry,* Vol. I, p. 43, was obtained by first treating the leaves with alcohol, then percolating them with hot distilled water, evaporating in vacuo to a syrup, precipitating and purifying by use of absolute alcohol, then drying the product in vacuo at 110 degrees F. The *ceanothine* thus prepared was said to be a dry mass, partly crystalline and when purified was white, had an odor like green tea, and was soluble in water but insoluble in alcohol. Bowman [1] determined tannin in a number of drugs and among them was Ceanothus. He reported 9.21 per cent. tannin. Clinch [2] examined the leaves. He obtained 5.64 per cent. benzole extract and in this extract he obtained tests for alkaloid. He also reported finding resin, fixed oil, and wax in this extract. In the alcohol extract (after exhaustion with benzole) he found tannin but no alkaloid. Gerlach [3] made a more thorough examination of the bark of the root. He found an aromatic fixed oil, wax, and traces of volatile oil in his petroleum ether extract. His ether extract contained resin. His absolute alcohol extract contained tannin, gallic acid, glucose, and a red coloring matter which he called ceanothus red. From this alcohol extract he obtained 0.2 to 0.3 per cent. of an alkaloid. He also extracted the drug with acetic acid and from this extract he reported finding alkaloid to the extent of 0.37 and 0.52 per cent. of the drug.



Crystalline Alkaloid. **Amorphous Alkaloid.**



Gold Salt of Crystalline Alkaloid. **Potassium-Bismuth-Iodide Salt of Crystalline Alkaloid.**

Picrate of Crystalline Alkaloid. **Picrate of Crystalline Alkaloid.**

He reported the alkaloid to be readily soluble in chloroform separating in "granular crystals" melting at 190 degrees C. He reported it less soluble in ether, alcohol, and carbon disulphide, to have a distinctly bitter taste, and to resemble caffein in not readily forming salts. He suggested the name *ceanothine* for this alkaloid. Buckner [4] examined the leaves but reported no alkaloid. Hitchcock [5] examined the root determining the per cent. of extractive by various solvents and reported resin, tannic acid, phlobophene, gums, mucilage, sugar, etc., but makes no mention of an alkaloid. Gordin [6] assayed the drug (entire root) by various methods and found 0.2 per cent. alkaloid. He separated the alkaloid by means of hot alcohol obtaining fractions melting at 227 degrees C. and 249 degrees C. By dissolving these in acid and precipitating with ammonia he obtained a snow white substance melting at 255 degrees C. This latter substance was soluble in alcohol with difficulty, almost insoluble in ether and formed picrates insoluble in alcohol. He obtained another white substance melting at 200 degrees C. which was too soluble to be crystallized from alcohol. It was also quite soluble in ether. The alkaloid (which one is not stated) formed gold and platinum salts, acetyl and benzoyl derivatives, and solutions in hot chloroform or benzole gelatinized on cooling. He stated that the alkaloid was readily extracted from the root by dilute acid or alcohol and that the acetate was less soluble than the chloride or sulphate.

Examination of the Drug (Bark of the Root)

In this investigation several different samples of the drug have been examined by the usual extraction with different solvents. The results are not of sufficient interest to warrant extended discussion. A peculiar aromatic pungent oil has been obtained, large quantities of what is called "resin" for lack of a better name are being preserved for future study. Tannin is readily obtained. A careful examination for glucosides did not result in any positive evidence of their presence although there is a suspicion of their presence.

Alkaloid

The presence of alkaloids is very readily established. Simple maceration of the ground material in acetic acid gives a solution which contains alkaloid. Extraction of the ground drug with ether, chloroform, or even petroleum ether removes distinct traces of alka-

loid. Extraction with ether, chloroform, acetone, or ethyl acetate in the presence of alkali, either ammonia or slaked lime, easily removes the alkaloid. Ethyl acetate seems to be the best solvent, acetone probably the next, then chloroform and ether. The U. S. P. method of assay removes the alkaloid readily. In all the extracts thus obtained the alkaloid is accompanied by a large amount of foreign material. This is mostly "resin" and a little oil. Alcohol of almost any concentration down to about 25 per cent. extracts the alkaloid readily but it also takes along with it so much coloring matter and other extractive that it has been practically impossible to devise a method to remove the alkaloid in a pure state from the alcohol extract.

If the ground drug is mixed with powdered lime, well moistened, and then dried and extracted in a continuous extraction apparatus with ether an extract is obtained which is quite free from color and contains the alkaloid together with oil and "resin." Other solvents mentioned above also remove the alkaloid but while longer extraction is required when ether is used the character of the extract is so much more suited to the removal of the alkaloid that this method has been used more frequently than any other. Ethyl acetate is excellent but in the presence of alkalies and moisture it is so readily hydrolyzed that it is difficult to keep a mixture alkaline when it is used. Ammonia may replace the lime but in a continuous extraction apparatus it is difficult to employ it.

The extract obtained in the above manner is usually semisolid or resin like and of a light brown color. The oil and fat which it contains may be removed by washing with petroleum ether although this causes some loss of alkaloid. After removal of this oil the mass can usually be reduced to a fine powder. From this powder the alkaloid is extracted by repeated washings with acid. Acetic acid seems to be the best suited to the purpose but a large number of extractions are required to remove all the alkaloid. In this process of extraction some of the "resin" is carried along with the alkaloid. Hydrochloric acid causes some decomposition of the material and dissolves more of the "resin." From the acid solution the alkaloid is readily precipitated by ammonia and it may be collected by filtration or by extraction with ether or chloroform. It is quite evident that by this method of isolation the alkaloid may contain some of the "resin" originally extracted and this will be referred to later on.

The alkaloid prepared in this way is usually quite white but in some cases has a slight yellow color and some samples have a peculiar pink or pale salmon color. It is odorless and has a bitter taste but not as decided as many alkaloids. It is not soluble in water to an appreciable extent. It dissolves very readily in alcohol but much less readily in ether and chloroform. Acetone and ethyl acetate dissolve it quite readily. All solvents such as benzole, xylol, toluene, amyl alcohol, butyl alcohol, etc., which have been tried dissolve it with varying degrees of ease and hot solutions, if saturated, gelatinize on cooling. In many cases by concentration of solutions in some of the above solvents, notably ether, and alcohol, a product has been obtained which is not crystalline but is remarkably uniform in appearance under the microscope. It is distinctly granular as shown by the photomicrograph. Nearly every attempt to crystallize this product failed, either a gelatinous mass resulting or the granular product. This product as isolated has a very uniform melting point. Perhaps fifteen lots have been prepared and the melting point always has been found to be very close to 190 degrees C. This led to the conclusion that Gordin's alkaloid which he reported as melting at 200 was being isolated. In the search for a crystalline alkaloid a product would occasionally be obtained melting somewhat higher than 190 even as high as 220 on a few occasions. Finally, one lot was obtained with a rather high melting point and from this by solution in hot normal butyl alcohol a fine crop of crystalline alkaloid was obtained. These crystals are perfectly white and have the form shown in the photomicrograph. On several occasions in the process of purification of the extracts prepared from the drug these same crystals were obtained in small quantities. All efforts to isolate them failed, however, as they invariably disappeared in the processes of purification tried.

Since no separate and distinct alkaloids could be obtained from the amorphous product by crystallization (except as noted above) recourse was had to "fractional solution" as a means of separating individual alkaloids if present. Since the material was known to be soluble in ether but not too freely so this solvent was used and the surprising results recorded below were obtained.

To 0.900 gm. of the material having a M. P. of 185 degrees C. was added 25 cc. of ether. The solution was decanted into a tared beaker and the ether evaporated. 0.240 gm. of residue was obtained. The process was repeated on the undissolved material and the second 25 cc. of ether dissolvd 0.183 gm. This process was

repeated until ten fractions were obtained. They were as follows: No. 1, 0.240 gm., No. 2, 0.183 gm., No. 3, 0.107 gm., No. 4, 0.083 gm., No. 5, 0.058 gm., No. 6, 0.042 gm., No. 7, 0.036 gm., No. 8, 0.029 gm., No. 9, 0.029 gm., No. 10, 0.021 gm. A small amount still remained undissolved. The first three lots were yellowish the remainder increasing in whiteness until the last ones were pure white. Every fraction was amorphous and those tried would not crystallize from hot butyl alcohol. Every fraction gave alkaloidal reactions but no microscopic crystalline salts with picric acid could be obtained from any of them.

This process was repeated a little more carefully starting with 0.959 gm. of a product melting at 185-190 C. and using 50 cc. of ether each time. The first 50 cc. of ether dissolved a large portion of the material (weight not noted) but this fraction had a melting point of about 140 degrees C. The second fraction (weight not noted) melted at about 160 degrees C. The third fraction weighing 0.065 gm. melted at 227 degrees C. The fourth weighing 0.050 gm. melted at 225 degrees C., the fifth weighing 0.034 gm. melted at 235 degrees C., the sixth weighing 0.031 gm. melted at 235 degrees C., and the seventh weighing 0.021 gm. melted at 232 degrees C. This seemed to indicate that the fractions 3, 4, 5, 6 and 7 were of uniform composition, and they looked alike. They were combined and the mixture melted at 225-227 degrees C. This mixture was then washed with ether four times and the insoluble residue melted at 235 degrees C. and the ether soluble portion at 183 degrees C. The residue (M. P. 235 degrees C.) was further washed with ether and the insoluble portion melted at 241 degrees C. All these products gave alkaloidal reactions and were amorphous. While not every one was tested those that were gave no crystalline picrate and none were found that would crystallize from butyl alcohol. The quantities were very small and the microscopic test with picric acid was depended upon for the detection of the crystalline alkaloid (see below under crystalline alkaloid).

This process was again repeated as follows: Starting with 0.8965 gm. material the first lot extracted weighed 0.370 gm., M. P. 160 degrees C., the second lot 0.230 gm., M. P. 177 degrees C., the third lot, 0.135 gm., M. P. 210 and the fourth lot 0.100 gm., M. P. 225 degrees C.

The above four lots were combined, dissolved as completely as possible in 50 cc. dilute hydrochloric acid (about 4 per cent.) and

the insoluble matter filtered off. To the acid solution was added silico-tungstic acid in excess, the precipitate collected and washed with dilute hydrochloric acid, mixed with water in a separator and made alkaline with sodium hydroxide. The alkaloid, which was abundant, was extracted with ether and the product thus obtained was almost pure white. It was then submitted to the same extraction process with ether. The first portion extracted melted at 180 degrees C., the second at 195 degrees C., and the third at 220 degrees C.

It had been noted that the melting point of the "resin" frequently referred to was quite uniformly about 125 degrees C. and attention has been called to its possible presence in the alkaloidal material as extracted by the process used. This resin is very soluble in ether and its presence would account for the low melting points of the first portions extracted in the above experiments. It was shown by actual trial that this resin, which dissolves to some extent in hydrochloric acid, does not precipitate with silico-tungstic acid. It is clear then that the silico-tungstic acid would precipitate alkaloid only, leaving behind the resin and if the low melting points of the first fractions were due altogether to this "resin" the alkaloid combining with the silico-tungstic acid should be pure and all portions of it have the same melting point. Instead, as noted above, one portion melted at 180 degrees C. another at 195 degrees C. and a third at 220 degrees C.

The only conclusion to be drawn from all the above is that the material so constantly obtained and melting at about 190 degrees C. is a complex mixture of alkaloids and in addition may contain some of the "resin" originally extracted from the drug along with the alkaloid.

The one lot of crystalline alkaloid obtained in quantity sufficient for examination was almost snow white, not so bitter as the amorphous mixture, practically insoluble in water and very much less soluble in alcohol than the amorphous. While no exact data can be given the solubility in alcohol of all the different products obtained seemed to decrease with increase in melting point. The same may be said of the solubility in ether. (It is possible that even by continuous extraction the ether used in the original extraction of the drug fails to extract this crystalline alkaloid, or failed to remove sufficient of it to make its subsequent recovery possible. This may explain the failure to isolate it in any considerable quantity. This

phase of the question will be more fully considered in the future.) These crystals melted quite sharply at 255 degrees C. They formed crystalline salts with picric acid, gold chloride, and bismuth-potassium-iodide but in all other respects reacted the same as the amorphous alkaloid.

A very thorough examination of the mixed alkaloids was made in an endeavor to discover any characteristics which they might possess. In what follows the word alkaloid refers to the amorphous mixture the crystalline alkaloid being referred to as such. Solutions in hydrochloric acid were made of both alkaloids in the proportions of 1:1000, 1:2500 and a "stronger" solution the concentration of which was not known. All the precipitates were produced and examined under the miscroscope following in general the plan of Stephenson, Microchemical Tests for Alkaloids, p. 11. The results are given in the following tabulation:

Reagent used.	*Amorphous Alkaloid*	*Crystalline Alkaloid*
Iodine in Potassium Iodide (Wagner's Reagent)	A.	A.
Potassium-mercuric-iodide (Mayer's Reagent)	A.	A.
Potassium-cadmium-iodide (Marme's Reagent)	A.	A.
Potassium-bismuth-iodide (Dragendorff's Reagent)	A.	C. Brick red crystals. Very small (?)
Zinc-chlor-iodide	A.	A.
Phosphomolybdic acid (Sonnenschein Reagent)	A.	A.
Phosphotungstic acid (Schleibler's Reagent)	A.	A.
Silicotungstic Acid	A.	A.
Picric acid (Hager's Reagent)	A.	C. See Photomicrographs.
Tannic acid	A. Only in strong solution.	A. Only in strong solution.
Chromic acid	No reaction	No reaction.
Mercuric chloride	A. Only in strong solution.	A. Only in strong solution.
Mercuric nitrate (Millon's Reagent)	A.	A.
Gold chloride	A.	C. Exceedingly small cubes (?)
Platinum chloride	A.	A. (?)
Potassium ferrocyanide and potassium ferricyanide	A. In acetic acid sol. only.	A. In acetic acid sol. only.
Potassium permanganate	Ppts., then reduces the Mn.	Ppts. then rapidly reduces the Mn.

A = amorphous. C = Crystalline.

Color reactions with nitric acid, sulphuric acid, sulphomolybdic acid, sulphovanadic acid, sulphoselenious acid, and bromine water were not sufficiently pronounced to be characteristic. Concentrated hydrochloric acid or the diluted acid when heated give a decided yellow color. Sulphuric acid-potassium dichromate mixture was rapidly reduced giving the typical green color of chromic compounds. Potassium permanganate in sulphuric acid was also reduced. Ferric chloride and potassium ferricyanide were rapidly reduced giving the typical blue precipitate. No murexide reaction could be obtained.

Summary

In this work it has been shown that Ceanothus americanus contains a complex mixture of alkaloids. Methods of extracting the alkaloids are discussed. One crystalline alkaloid was isolated. The reactions of the alkaloids, both the mixture of amorphous ones and the crystalline one, towards a number of alkaloidal precipitants has been recorded and photographs of the few crystalline precipitates obtained, all from the crystalline alkaloid, have been made. The common color tests were tried but no characteristic reactions were obtained. An interesting resin like substance is reported upon very briefly.

Acknowledgment is made to Professor C. C. Glover of the University of Michigan for advice and encouragement throughout the progress of the investigation.

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APPLICATION OF MICRO METHODS TO CONTROL WORK IN PHARMACEUTICAL MANUFACTURING

Dr. William Figdor

Plaut Research Laboratory of Lehn & Fink, Inc., Bloomfield, N. J.

IN A preliminary paper* W. H. Gesell and M. A. Dittmar of this laboratory pointed out the economies that might be realized by practically applying micro-chemical methods in the control laboratory. The author of this paper has taken up this investigation and reports his results in the following pages:

The experiments carried out convinced him that micro-methods were capable of giving accurate results in the hands of the average careful analyst. Of course, it is obvious that careless work is fatal to successful results by this method since the error is magnified.

For practical micro-control work a good analytical balance of 1/10 mg. sensitivity can satisfactorily be used.

The value of micro-chemical work to any particular laboratory must be decided by local needs. Some methods while giving accurate results offer no economy as regards time. Where material is precious, the value of a saving in this direction is obvious. On the other hand in the laboratory where a large amount of routine analyses are run, a substantial saving in time will also be of great value in reducing costs.

The following represent methods and results which were obtained by the author in carrying out his investigation. Some of the figures in the tables of assay results include those published in the previously published paper.

Determination of Alkali Earth Salts of Organic Acids

Since the assay prescribed in the U. S. P. proved to be very long and cumbersome, a modification of F. Pregl's method was used. This permitted using a platinum crucible of usual size.

Four-hundredths to eight-hundredths gram of organic salt is weighed in a platinum crucible and moistened with a few drops of sulphuric acid. Then the crucible is covered and the contents ignited with a flame from above in such a way that the vapors of sulphur

*Micro Chemistry as an Industrial Economy. *Journal of Industrial & Engineering Chemistry*, vol. 17, No. 8, p. 808 (1925).

dioxide are soon evolved. As soon as the sulphuric acid is evaporated, the contents of the crucible are examined. If not absolutely white, add a few drops of sulphuric acid and evaporate again. This is only necessary in the case of salts with a high carbon content. If the contents are white, add a few granules of ammonium carbonate and ignite (the crucible) at dull red heat for several minutes. Then let cool and weigh. Add again a small granule of ammonium carbonate and ignite as before. The weight of the crucible must be constant. Constancy of weight ought to be reached after the second ignition.

In the following, and also in the subsequent tables, a comparison of results obtained using both micro and macro methods is given:

	Micro %	*Macro* %
Lithium citrate	99.08	99.77
Potassium citrate	99.42	99.6
Sodium salicylate	99.08	99.21
Sodium benzoate	98.4	98.8
Sodium acetate	99.85	99.85
Sodium benzoate	99.26	100.0

Quantitative Micro Ash Determination of Drugs

The correctness of the results depends to a great extent on good sampling. It is therefore important to grind the drug as finely as possible so as to get a good sample. The ash determination was done in F. Pregl's micro muffle in a small platinum boat. A very brief method is suggested below. The platinum boat containing the sample (20-40 mg.) is held with tweezers over a Teclu burner and carefully ignited. This ignition is complete in two minutes. It otherwise requires ten minutes.

	Micro %	*Macro* %
Spanish Saffron	5.21	5.22
Rhubarb root	3.72	4.2
Licorice Spanish	7.45	7.5
Gelatine	1.99	1.98
Arnica flowers	7.79	8.02
Low mallow leaves	16.5	16.58
Valerian root	11.08	11.58
Agar Agar	2.9	2.95
Senega root	3.9	3.25

	Micro %	*Macro* %
Ginger root	3.26	3.21
Anise seed, Spanish	8.61	7.54
Black cohosh root	5.31	5.94
Agar Agar	3.71	3.72
Valerian root	6.67	6.74
Orris root	1.99	1.79
Anise seed	6.21	6.41
Chamomile flowers	10.44	10.5
Poke root	9.4	8.89
Poson oak	4.38	4.82
Hyoscyamus	19.33	19.3
Cardamon seed	3.79	3.91
Nux vomica	3.13	3.27
Euphorbia piluifera	7.65	7.65
Bryonia root	8.44	8.83
Chestnut leaves	3.82	3.53
Gentian root	3.81	4.28
Bitter Orange peel	3.91	4.04
Orris root	2.29	2.60
Insect flowers	5.85	5.82
Juniper berries	2.85	2.88
Coriander seed	4.83	5.14
French thyme	7.0	6.87
Hyoscyamus	19.33	19.30
Angelica root	13.81	14.37
Lobelia herb	6.55	6.56
Valerian root	9.47	9.64
Gentian root	3.68	3.91
Ginger root	2.95	2.93
Boneset herb	7.32	7.31
Sarsaparilla	7.62	7.7
Chamomile flowers	11.4	11.8
Wormwood	12.4	11.96
Yellow Mustard	4.52	4.31
Larkspur seed	4.97	4.93
Juniper berries	2.53	2.75
Mallow leaves	16.39	16.50

Determination of Residues in Tinctures and Fluid Extracts

Two cc. of the preparation are evaporated in a silica or porcelain dish using the steam bath. After five minutes the evaporation residue can be transferred to the drying oven. Dry at 110 degrees C. for about three hours. The weight must be constant.

	Micro %	*Macro* %
Tr. Guaiac	18.81	18.814
Tr. Belladonna leaves	2.71	2.61
Tr. Kino	8.56	8.1
Tr. Benzoin Compound	16.72	16.03
Tr. Myrrh	7.85	7.7
Tr. Arnica flowers	4.13	4.08
Tr. Cascara Sagrada	25.1	24.3
Tr. Cascara Sagrada	23.5	23.2
Tr. Cascara Sagrada	59.7	60.0
Tr. Cascara Sagrada	57.3	57.3
Fluid Extract Gentian	11.53	11.17
Fluid Extract Gentian	23.3	24.0

Determination of Esters and Menthol in Oil of Peppermint

The assay of esters was carried out by the U. S. P. method, but the tests were made with only 2 cc. of oil.

Method for esters: 2 cc. of oil are weighed out into a 50 cc. flask and 10 cc. of a n/10 alcoholic KOH are added. Heat for half an hour under reflux and titrate with n/10 H_2SO_4 and phenolphthalein.

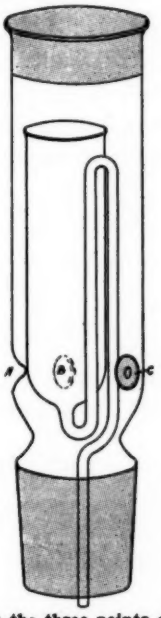
Method for Menthol: 2 cc. of oil are mixed with 5 cc. acetic anhydride, 0.5 gram of sodium acetate in a small 50 cc. acetylization flask and boiled for one-half hour. Then the mixture is washed in a separatory funnel with sodium carbonate and then with water till the water gives a slight alkaline reaction. The oil is then dried and weighed. The rest of the procedure is as under esters.

Ester (Menthyl Acetate) Micro %	*Ester (Menthyl Acetate) Macro* %	*Menthol Micro* %	*Menthol Macro* %
11.60	10.75	62.3	62.3
12.79	12.25	66.33	62.1
10.45	9.86	60.12	60.4
7.84	7.45	65.26	66.0
9.64	9.39	57.87	57.3
11.4	11.04	60.78	61.3
22.54	22.00	59.4	58.9
9.39	9.15	76.51	76.9
10.15	10.12	45.26	45.00
		63.33	62.1

It has also been found that the U. S. P. test for the detection of dimethyl sulphide can be replaced by one far more sensitive. 0.5 cc. of the original oil is poured on 2 cc. of Nessler's reagent. A yellow zone or a yellow precipitate indicates dimethyl sulphide. No preliminary concentrating is necessary. The specific gravity is determined with 2 cc. of oil.

Determination of Non-Volatile Extractive Soluble in Ether or Petroleum Ether

The U. S. P. method was applied using 1 gram substance and 150 cc. of solvent only. Seven hours are sufficient for the extraction. Generally speaking, it is possible to reduce the time of extraction by reducing the amount of the drug to be extracted. It is further necessary to raise the temperature to which the extraction thimble is exposed. For this purpose a Soxhlet apparatus was used, the thimble of which was continually heated by the ascending vapors of ether or petroleum ether. As long as the extracting matter is not destroyed by heat, this method is usable. Flaxseed, ginger root and cinnamon bark were analyzed by this method. The following is a sketch of the Soxhlet apparatus:



A, B, C are the three points on which the thimble reposes.

Determination of Alkaloids in Drugs and Alkaloidal Preparations

When controlling the methods of H. Dieterle (Archiv der Pharmazie 1923, Band 261, p. 77 ff.) it was found that the mixture of ether and petroleum ether recommended by Dieterle for the extraction causes the formation of an emulsion which takes a very long time to separate. As soon as the solvent was changed, good results could easily be obtained.

Ipecac Root and its fluid extract: Shake about 0.5 gram of finely ground Ipecac Root for 10 minutes with a mixture of 10 cc. Na_2CO_3 solution plus 15 cc. of ether. Add 0.3-0.4 gram of tragacanth, and shake out with ether until the alkaloid reaction disappears (3 or 4 times). Evaporate the ether extract, add 5 cc. n/10 H_2SO_4 and titrate back with n/10 KOH and methyl red as indicator. The fluid extract is treated in the same way. Two cc. of fluid extract is sufficient. (1 cc. n/10 H_2SO_4 = 0.02482 gram of alkaloids.)

	Micro %	*Macro* %
Root	3.09	3.12
Fluid Extract	1.36	1.40

Tincture of Nux Vomica: Shake 2 cc. of the tincture with 10 cc. of chloroform, 2 cc. 10% NH_4OH plus 2 cc. H_2O and shake 15 minutes. Add 0.2 gram of tragacanth and separate in a separatory funnel. Shake the mixture three times more with 10 cc. of chloroform, separate and evaporate. Add to the dry alkaloids a little ether and 5 cc. of n/10 H_2SO_4, evaporate the ether and titrate back with n/10 KOH. (1 cc. of n/10 H_2SO_4 = 0.0364 gram of alkaloid.)

I In 100 cc. 2.32 grams of alkaloids-micro
In 100 cc. 2.30 grams of alkaloids-macro
II In 100 cc. 1.93 grams of alkaloids-micro
In 100 cc. 1.86 grams of alkaloids-macro

H. Dieterle's methods for testing Morphine in Opium did not give the expected results.

ON THE INSTABILITY OF THE SODIUM SALT OF BENZOYLHYDROGENPEROXIDE

By

Arnold J. Gelarie, M. D., New York,

and

Frederick R. Greenbaum, D. Sc., Philadelphia

IN THE course of a pharmacological investigation, we had an opportunity to study the very interesting but very unstable sodium salt of benzoylhydrogenperoxide. This compound has the following formula: C_6H_5 CO O_2Na. Its free acid which can be obtained by acidifying with sulphuric acid has the composition C_6H_5 CO O_2H.

It can be regarded as hydrogenperoxide, in which one hydrogen atom is replaced by the benzoyl group. In its behavior, the benzoylhydrogenperoxide is a very powerful oxidizing agent standing between Caro's reagent on the one hand and hydrogenperoxide on the other.

The preparation of this compound was carried out according to the method of Beyer & Villiger,[1] using benzoylperoxide as starting material. The benzoylperoxide was prepared from benzoylchloride in the following way:

Commercial benzoylchloride is gradually added with continuous stirring to a solution of sodiumperoxide, care being taken that this solution be thoroughly cooled with ice, as the reaction between benzoylchloride and sodiumperoxide is very violent, occasionally resulting in a flame. The addition of benzoylchloride is continued until the white precipitate which forms no longer increases and the typical odor of benzoylchloride disappears.

The formation of benzoylperoxide from benzoylchloride occurs according to the following equation:

$$2\ C_6H_5CO\ Cl + Na_2O_2 \rightarrow (C_6H_5\ CO)_2\ O_2 + 2\ Na\ Cl.$$

This white precipitate is filtered, washed with ice water, and crystallized from boiling alcohol. It crystallizes in fine white needles.

The benzoylperoxide so obtained has a melting point of 103 C., is insoluble in water and soluble in boiling alcohol and ether.

This benzoylperoxide is now dissolved in ether and, according to Beyer & Villiger,[1] treated with an equimolecular portion of sodiumethylate. The sodiumethylate reacts with the benzoylperoxide and forms the sodium salt of benzoylhydrogenperoxide and ethyl ester of benzoic acid, according to the following equation:

$$(C_6H_5CO)_2\ O_2 + C_2H_5O\ Na \rightarrow C_6H_5\ CO.\ O_2Na + C_6H_5CO\ O\ C_2H_5.$$

Four gr. of pure benzoylperoxide are dissolved in 200 cc. of ether and to this solution sodiumethylate is added, which is prepared from 0.38 gm. of metallic sodium and 10 gm. of 95 per cent. alcohol. The sodiumethylate, when cold, is added gradually to the etherial solution of benzoylperoxide. A white precipitate is obtained. As this precipitate is too unstable to be filtered, being especially unstable when dry, we dissolve this precipitate in water. About 25 cc. of water are enough to dissolve it and give a 14 per cent. solution. This has an alkaline reaction and on the addition of an acid, a precipitate of an acid salt is obtained at first. On further addition of acid, the free benzoylhydrogenperoxide is precipitated. It can be isolated by washing first with ether to free it from the benzoicethyl ester, then by taking up with chloroform and drying with anhydrous sodiumsulphate. On evaporating *in vacuo* crystals of benzoylhydrogenperoxide of a melting point of 41-43 degrees C. are obtained.

In contact with water benzoylhydrogenperoxide gives an oil of an odor like hypochloric acid. As however it is almost insoluble in water, although soluble in ether, we could not use this compound for our purposes and had to use the sodium salt. It seems that the free benzoylhydrogenperoxide is much more stable than the sodium salt.[2]

The sodium salt of benzoylhydrogenperoxide has the tendency to give off oxygen and is transformed into the more stable sodiumbenzoate, according to the following equation:

$$C_6H_5\ CO\ O\ O\ Na \rightarrow C_6H_5\ COO\ Na + O$$

This oxygen is in the *status nascendi* and has a very great oxidizing power. On standing a solution of sodiumbenzoylperoxide loses its activity, that is the free oxygen decreases more and more, and after about forty-eight hours the decomposition of the sodiumbenzoylper-

oxide into sodiumbenzoate and oxygen is complete, so that after standing for about two days it contains only sodiumbenzoate. The decomposition is accelerated by the presence of foreign substances. This behavior is very similar to that of hydrogenperoxide, only the latter substance is more stable and its decomposition takes place much slower, especially in the presence of acetanilid, when it can be kept unchanged for several months. The sodium salt of benzoylhydrogenperoxide is, however, very unstable in the presence of any foreign substance, particularly reducing agents.

A characteristic reaction for this compound, which can be used to determine the degree of decomposition is its behavior towards potassiumiodide. If a solution of the sodium salt of benzoylhydrogenperoxide is acidified and potassiumiodide is added, black, metallic iodine is precipitated, provided the sodium benzoylhydrogenperoxide was freshly prepared. If, however, the sodium benzoylhydrogenperoxide has been allowed to stand for several hours or for twenty-four hours, then the solution, after the addition of potassiumiodide turns dark brown, light brown or yellowish, depending upon the degree of the decomposition of the sodium benzoylhydrogenperoxide. Therefore, the quantity of iodine precipitated can be a measure for the degree of this decomposition.

The amount of iodine can be determined quantitatively by titration with a sodiumthiosulphate solution of known strength. In this way the concentration of freshly prepared sodium salt of the benzoylhydrogenperoxide and the degree of decomposition with time was studied.

We found that the pure compound dissolved in water is decomposed in the course of twenty-four hours to about 95 per cent. and that after forty-eight hours the decomposition was complete. Furthermore we found that foreign substances like urea, quinine, hexamethylenetetramine, copper sulphate, sodium cinnamate or fatty acids in form of their water soluble sodium salts, such as soaps of castor oil, cod liver oil or olive oil, chaulmoogra oil, accelerate this decomposition of the compound.

The following table shows the decomposition of sodium benzoylhydrogenperoxide with time and different foreign substances:

Experiment No.	Compound used	Per cent. when freshly prepared	Per cent. after 2 hours	Per cent. after 24 hours	Per cent. after 48 hours
1	Sodium salt of benzoylhydrogenperoxide alone	3.42	2.7	0.02	0
2	the same	3.30	2.7	0.43	0
3	Castor oil soap & benzoylhydrogenperoxide	0.76	0.74	0.34	0
4	Chaulmoogra oil soap & benzoylhydrogenperoxide	.8	0.76	0	0
5	Olive oil soap & benzoylhydrogenperoxide, sodium	0.74	0.74	0	0
6	Cod liver oil soap & benzoylhydrogenperoxide	1.1	1.0	0.19	0

From this table we can see that any one of the soaps used decrease the concentration of the benzoylhydrogenperoxide from 3 per cent. to below 1 per cent. in two hours, and that after twenty-four hours decomposition has proceeded to about 95-99 per cent. and is completed in forty-eight hours.

Just as hydrogenperoxide acts as an oxidizing agent and at the same time as a reducing agent, so also does the sodium solt of benzoylhydrogenperoxide not only act as an oxidizing agent but also as a reducing agent. For instance, potassium permanganate in acid solution is oxidized to manganese dioxide, and gold salts are reduced to metallic gold.

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SOME INSECTS AND THEIR RELATION TO MAN*

M. A. Reasoner, B. S., M. D., F. A. C. S.,
Major, Medical Corps, U. S. Army

FROM THE beginning of history to the present time man has been a prey to insects and consequently a sufferer from diseases which they are capable of transmitting. It is impossible to estimate the effect which this insect activity has had upon the human race.

If one were asked to name the safety device which has come into common use during the last half century which has saved the greatest number of lives and prevented the greatest amount of illness which could not otherwise have been prevented, one would be quite safe in designating the ordinary fly and insect screening. It is quite probable that most of us do not realize many of the advances we have made in controlling the spread of insects because we are very prone to accept new comforts and forget former hardships as well as the lessons connected with them. We do not commonly think of the important part which insects have played in history, how they have overthrown dynasties and even wiped out whole countries or civilizations or reduced them from a position of commanding superiority to one of helpless subordination. They have defeated victorious armies on the way to conquer the world and at times have allied themselves with the defeated who were thus able to turn inglorious defeat into substantial victory. It is only in the last forty years that we have begun to comprehend and thereby raise ourselves to a plane superior to our insect and other untoward surroundings, and the fly-screens, the insecticides, the disinfectants and the appurtenances thereto are the symbols of our long deferred superiority and victory.

Five hundred years before Christ, or about the time of Pericles, Greece was the center of power and of culture and intelligence. It was only a few years later that the anopheles mosquitoes of the country became in some manner infected with malaria, called by Hipporates "the burning disease," and the country began immediately to decline and never again was a predominant factor in the history of the world. The disease became general and was sufficient to produce a physical and mental deterioration in one of the strongest and most virile nations the world has produced. Today malaria is one of the

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great problems in Greece and when this condition is overcome there should be an improvement in their mental and physical condition though some time and doubtless some new blood will be required to overcome the results of two thousand years of malarialization.

Mesopotamia up to 500 B. C., had a relatively high degree of civilization but became weakened by the constant fight against malaria so as to become what might be termed a "low vitality" nation. It thus became invaded and captured by enemies from the higher lands who in turn suffered the same fate.

Egypt also a "low vitality" nation had developed a high type of civilization and culture but fell a prey to malaria, typhus, bubonic plague and other insect transmitted diseases. Following this decadence, it endured a regular succession of conquerors, each in his turn succumbing to the same insect borne diseases which had overcome his predecessor.

As with the preceding countries, Macedonia had built up a civilization of its own but fell in the same manner and at the present time is still in the grip of this curse of anopheles mosquitoes which make civilized life and proper mental and physical development impossible. During the War, there were about 750,000 allied soldiers in Macedonia and of this number about one-half were infected with malaria and any army with one-half its number on sick report has neither time nor ability to accomplish much else. It might also be said that any country so infected is hardly worth fighting over.

During the last few years we have begun to explore the numerous and extensive ruins which are the only remains of former civilizations once existing in the southern part of Mexico, Central America and Peru. The Mayans inhabited the country in and about Yucatan and at one time their main city Chichen Itza, was the largest city in this hemisphere. Malaria and yellow fever appeared and this strong country began to degenerate until it was no difficult matter for the Guatemalans to come down from the higher lands about one hundred miles away and capture the country. The Mayans left behind them traces of a civilization which showed advanced knowledge of astronomy, chronology, mathematics and architecture but unfortunately for them they never learned that the stegomyia mosquito is responsible for the transmission of yellow fever and the anopheles for malaria.

Following the decadence of Greece, Rome made itself the world power but along with other factors the insects soon made themselves

manifest. The anopheles mosquitoes throughout Italy became infected with malaria possibly through travelers from Greece who had been infected there and carried the organisms in their blood. The disease soon became epidemic in the low lands and especially in the region in and around Rome. The traders and crusaders all carried their full quota of insects and so in addition to malaria they had frequent epidemics of bubonic plague, typhus and relapsing fever with an assortment of contact and fly borne diseases and Rome was on the downward path. But as frequently happens the insects became not only their enemy but their ally as well. In 936 A. D., the Emperor Otto attacked Rome and while his initial military operations were successful yet his army soon became infected with a severe insect borne epidemic which destroyed his military preponderance. Henry IV of Germany captured Rome in 1081 and the insects then proceeded to put his army out of business. In 1137 A. D., Lothar invaded Italy but in a short time the malaria was too much for him and his army. In 1167 A. D., Frederick Barbarossa captured Rome after a decisive victory but his army because infected with both malaria and bubonic plague, caused by mosquitoes and fleas respectively. The Romans rallied and destroyed the sick and what was left of the well, and Frederick was fortunate in escaping with his life.

The armies of the crusaders probably fared worst of all from the insect borne epidemics, particularly in the first, the third and the seventh or last. It was not, however, the loss of life among the members of the crusades which was so important but the fact that as they traveled along the way and returned to their homes, those who did return, they distributed the infected insects they carried with them or, infected insects already there with the diseases they carried and as a result these epidemics became general through what was then the civilized world.

During the Thirty Years War as well as many others there was a far greater loss of life due to the transmission of disease through insects than that due to battle casualties.

In a similar manner to the countries already mentioned, may be explained the decadence of the civilizations once attained in Southern Arabia, Peru, Rhodesia, Ceylon, Java, Indo-China and India. In the Bible we find records of plagues, we find the same in Egyptian hieroglyphics, in the Assyrian and Phoenician records and in fact all history is full of such occurrences. The course of the world

has been changed and altered, and changed again beyond our power to estimate by these vast plagues of disease and often a humble and despised insect has been the cause of the trouble.

It is not many years since the interior of Africa was an unknown wilderness. Within this country was an area in which the dreaded African sleeping sickness was present. The natives did not travel far from home. The Tsetse fly which transmits the disease did not move far from its habitat along the water's edge and only the wild animals which harbor the parasite moved to any extent. But along came civilization and trade channels were opened up and the natives began to move around with caravans, and the wild animals were disturbed and compelled to seek new ranges, and at the present time the infection has spread over at least one-fourth of the continent and thousands of miles have become depopulated. The percentage of fatal cases in this disease is very high if untreated or not treated early. At the present time it is dangerous to pass through the highly infected regions and a sufficiently prolonged residence generally results in infection. It is not possible to kill all of the Tsetse flies nor to destroy all of the wild and domestic animals which harbor the parasite. It is quite probable that the disease has been in the United States during the olden slave days but there was no Tsetse fly to transmit it to animals which serve to keep it going and serve to infect other flies, which in turn infect human beings. It is to be hoped that this fly will never gain access to this continent.

I have read with great interest DeFoe's account of the great plague in London. I do not believe it is possible for us to conceive of the horrors these people underwent and therefore we are perhaps not properly appreciative of the blessings which have come to us as a result of the advances which have been made in the field of preventive medicine and sanitation. In my estimation this is the outstanding achievement of the century beside which other developments are not to be compared. These facts and procedures have not evolved themselves but are the results of the co-operation of bacteriologists, zoologists, hygienists, physicians, chemists, manufacturing chemists, and others. Here in the United States and in certain parts of Europe, the principles of preventive medicine have become so well established that the measures to be employed are generally known and have become incorporated into the municipal and other laws. The procedures which we consider as obvious and a matter of course are entirely unknown over a considerable portion of the earth. There

are languages and dialects which have in them no words corresponding to disinfectant, insecticide, antiseptic, etc.

It was a difficult matter to establish the proper sanitary measures in Cuba, Panama and the Philippines and secure their general observance. It has been a matter of years to train these peoples and even now they are prone to relax their care and ignore the fundamental rules which are instituted for their own good. It, therefore, requires constant watching and pressure upon our part to maintain hygienic conditions and prevent, so far as it is possible, the needless presence of easily preventable diseases.

Some years ago a small epidemic of cholera started in one of the Philippine villages. Word was sent out to establish a quarantine. When the health officers arrived the local health officer was requested to detail the measures which had been taken. He said he had established a quarantine and took them down to the bank of the river where he proudly showed them an American flag floating from a newly erected flagpole, which was his idea of a quarantine. He failed to grasp the idea of what was being attempted and that is the point of this tale.

The proof of the intelligence of a race is their ability to raise themselves above and protect themselves from adverse environment. The Nordics have shown themselves able to do this and were the first to gain a substantial victory in the continual fight against insects and this is, I believe, one of the important manifestations of their superiority. The average expectancy of male life in the United States is about 50.6 years and in Sweden is about 50.9 years. In India it is about 23 years and it would be less if the population were greater or the birth rate were higher. The combination of insects, ignorance and insanitation is the explanation. As an indication of what can be accomplished, the African Gold Coast annual death rate from 1881 to 1897 was 75.8 per thousand. In 1911 it had been reduced to 13.9 per thousand and the reduction was practically all in insect borne diseases.

It would be interesting if some students of history were to cite us to any instances of where the inhabitants of the tropics or lowlands had defeaed those from the highlands or colder climates on anything like equal terms. Such instances would certainly be in the minority. We ordinarily think of mountaineers as hardy and vigorous people and the residents of the tropics as lacking in strength and stamina. Unquestionably there is a climatological reason for

some degree of difference but there is another and possibly more important element. The resident of the tropics who does not protect himself, is engaged in a constant conflict against insects and the parasites which they transmit and as a consequence his vitality becomes lowered or he becomes the victim of disease. Man can not continue for generation after generation upon a low plane of vitality without degeneration and decadence, physically, socially, mentally and morally. It has, however, been shown that under proper precautions, inhabitants of temperate regions may emigrate to the tropics and live there without manifest injury. This requires the avoidance of mosquitoes and other insects, the constant use of boiled water and many other precautions which at times are somewhat irksome. Those who comprehend their importance are less likely to ignore them.

Some of us may remember the days when yellow fever was the curse of the tropical and semi-tropical western hemisphere. Some of us may remember or have heard of the consternation which was caused at the times when it gained a foothold in the United States. When we entered into war with Spain and invaded Cuba this was the greatest obstacle with which we had to contend. The Medical Department realized that the first step in the control of the disease was to learn the method of transmission and accordingly work was begun under the direction of Drs. Reed, Carroll, Lazear and Agramonte. In order to test all the various theories of transmission, volunteers were called for from the soldiers and officers of the Medical Department who were not immune to the disease. Attempts were then made to inoculate them with the disease by all of these various means and eventually it was found that the stegomyia mosquito, which had bitten a yellow fever patient during the first three days of the disease, was capable of transmitting it after a period of twelve days had elapsed. I think you will agree with me that a considerable degree of courage was required by these volunteers and those who lost their lives are entitled to all the honor which can come to any soldier who has fallen on the field of battle. As a result of this work we now know how to prevent the spread of yellow fever and as a consequence it has almost disappeared. It is the plan of the Rockefeller Foundation to destroy all foci of yellow fever and wipe it from the face of the earth and it seems very probable they will succeed in their endeavor. During the last few years Professor Noguchi of the Rockefeller Institute has been studying yellow fever and has in fact isolated the germ which causes it but he has had some

difficulty in securing a sufficient number of infected cases to work with.

The diseases which are transmitted by mosquitoes are malaria, yellow fever, filariasis and dengue fever. Malaria and yellow fever require no further mention. In filarial infection the mother organism locates itself in the lymphatic structures and gives birth to small motile organisms which occupy the blood channels by night and by day retreat to the liver or spleen. There may be no manifestations or there may develop a condition known as elephantiasis which is manifested by extreme enlargement more particularly in the lower extremities and may totally incapacitate the unfortunate victim. Dengue fever is also known as breakbone fever and is quite common in the Philippines and other portions of the tropics. It is not commonly fatal but is extremely painful and unpleasant to those who become infected.

The general rules to be followed with mosquitoes are as follows:

(a) Prevent so far as possible all mosquito propagation.
(b) Kill all mosquitoes possible of those which do breed.
(c) Keep habitations away from mosquitoes and mosquitoes away from habitations.
(d) Protect the sick from mosquitoes.
(e) Protect the well from mosquitoes.

It was the application of the above rules which made the building of the Panama Canal possible and life there as safe as in the temperate zones.

With us there is no question but that the common house fly is the most frequent tranmitter of disease. There ar also biting flies which are responsible for the spread of other diseases. Among the diseases which the domestic fly carries are typhoid fever, cholera, amebic dysentery, bacillary dysentery, gangosa and oriental sore or Bagdad boil. In the first four diseases the fly transmits the infection by carrying organisms from the discharges of the sick to the food of the well. These diseases may be transmitted by other means but the fly is a common method. These four diseases are all death producing and have been the cause of countless deaths. The latter two diseases are relatively unimportant and are only found in a few places in the tropics.

Obviously it is desirable to accomplish the same ends with flies as with mosquitoes though different methods are necessary. With

the partial disappearance of the horse from crowded communities, the problem of the fly has become less difficult. Screens are of course a necessity to prevent their access to the sick and the well and to food supplies. All infected discharges from the sick should be sterilized before being disposed of. Fly swatters, fly paper, fly poison and traps all have their places.

It may be a matter of interest to know that there are relatively few flies in the Philippines and the reason is that a variety of ants of which there are countless numbers, prefer the fly larvae as food and in that manner are of great assistance to the sanitarians and the general health of the islands.

There are a number of cousins of the domestic fly which cause harm and the following diseases are transmitted by them: yaws or framboesia, filariasis, Tuleremia or deerfly fever, cutaneous tropical myiasis and African sleeping sickness. Yaws is widespread throughout the tropics. It is manifested by sores over the body. It causes much invalidism but rarely ends in death. The type of filaria transmitted by the fly is very similar to that transmitted by the mosquito. Tuleremia is a disease which is found in parts of Utah. It is accompanied with high fever and is carried by a horsefly. Certain biting flies deposit their eggs beneath the skin of man and when this happens the results may be exceedingly serious. The African sleeping sickness has already been mentioned and is the most serious of this list. Obviously these diseases are difficult of control because the flies responsible are not domestic and it is impossible to entirely control their spread and propagation. One can not always stay behind screens, and headnets and gloves have their objections.

There are three kinds of fleas divided into those which live on the rat, those which live on the dog and those which live on man. They prefer their particular host but if compelled by hunger will go to another. Fleas transmit bubonic plague, and Leishmaniasis or dum-dum fever.

Bubonic plague might be described as a disease of rodents, more particularly the rat and squirrel which may be transmitted to man by means of the flea which serves as an intermediate host. It may be either an acute or a chronic disease in the rat, but when the latter dies, as it may with the acute type, the flea is compelled to seek another home. In the absence of rats it may settle upon a man, which is unfortunate for the man. It is easily understandable why once this disease has started it is difficult to stop. A good description of

an epidemic is to be found in 1 Samuel, 5th and 6th Chapters. The expatiation required of the Philistines was that they return the Ark of the Covenant to the Israelites along with five golden emerods or images of the characteristic swellings of the disease and five golden mice (or rats) the basis of the disease. It is interesting to know that the reference was called to the attention of Dr. Yersin at the time he was working out the cause and method of transmission of the plague. During the reign of Justinian it was responsible for as many as 10,000 deaths in one day in Constantinople and it was this disease which was responsible for the first attempt at a quarantine in Europe. It is continuously present in China and there is a constant focus of infection in Mesopotamia and the Himalayas. This is the disease which was known as the Black Death of the fourteenth century.

The dog, cat, ferret and weasel are the natural enemies of the rat and may be used in the campaign against him. All dumps should be eliminated, all drains should be screened, all food supplies should be protected and all places cleaned up which might harbor them. There are many poisons suitable, among them barium carbonate is the least toxic to man. Fleas are killed by a heat of 114 F. In a closed container sprinkled naphthalene will kill them in twenty-four hours. If dissolved in benzene and used as a spray it will kill them instantly. Sulphur and hydrocyanic acid gas are also efficacious. Fleas may wander back and forth to a certain extent from the dog to the rate and vice versa and here is a possible complication which must be considered. It is easy enough to deflea a dog but it may be equally easy for him to find others to take their places.

Leishmaniasis and dum-dum fever are confined to certain areas in the tropics and not of so much importance to us. It should be remembered that on more than one occasion, plague has obtained a foothold in the United States and was only overcome at the expense of considerable time and money and a few deaths.

Lice are prolific transmitters of disease. It is rather difficult for us to comprehend the attitude of mind of a few centuries ago which so calmly accepted these various pests as dispensations of Providence and unavoidable. The Buddhist religion which has millions of followers, teaches that no animal life should be destroyed. For this reason these people are always a potential menace to the remainder of the world from which it is difficult for us to thoroughly protect ourselves. The spectacle of a Buddhist priest engaged in picking

"cooties" from his body and laying them gently upon a stone from which they migrate back again to his body has always to my mind given a perfect demonstration of the word "futility." The diseases more commonly transmitted by lice are: Typhus fever, trench fever, and a form of relapsing fever.

Typhus fever is common over the world but the last thirty years has seen little of it in the United States, though still present in Mexico. This is a very fatal disease and during the Middle Ages and earlier when the louse had a higher standing in polite society, was the cause of many epidemics and great loss of life. Indian relapsing fever and trench fever, which are not so important to us, are carried by this insect. For a discussion of the means employed to get rid of "cooties" the reader is referred to any member of the A. E. F., who will doubtless do justice to the subject.

The tick is not a very common insect in settled parts of the United States but nevertheless it is at times exceedingly pernicious. Rocky Mountain spotted fever is prevalent in certain parts of Wyoming and Idaho and in the former state is accompanied by a mortality of from 75 to 90 per cent. In Idaho it is not nearly so fatal. The tick transmits this disease from squirrels and rats to man. The East and West African and the Persian types of relapsing fever are also transmitted by a tick. In the latter case these insects hide in the crevices and cracks of the house and at night come out and feed upon the sleeping persons and thus infect them.

The bedbug is responsible for the transmission of the European type of relapsing fever which is found especially in Russia. This universal nuisance is of course handled by standard means with which perhaps some of you are familiar. However, the traveller in infected districts may find it difficult to avoid an infection. Fortunately with the discovery of salvarsan, we have a specific for this disease. This same remedy may be used with equally good results in yaws, gangosa and the other forms of relapsing fever.

There are other diseases for which insects are responsible but those detailed are the more important ones.

There is a final thought which I wish to present to you. I can not help but believe there is a certain beneficent effect which results to the human race from the possibilities of epidemics, plague and transmissible diseases. When any collection of people or any country so far degenerate as to lose all desire for cleanliness and hygiene and proper living and subsist in dirt and filth, it is only a question

of time until an epidemic comes along and kills them off. In the meanwhile their resistance and bodily vitality has been reduced to the extent that with the increased amount of preventable disease there is a high death rate among adults, a higher death rate among infants, a lower birth rate and they go backward. Unfortunately it happens with the workings of nature's laws that the innocent must suffer with the guilty. I am of the opinion that even without any disease at the beginning, it would only be a question of time until a multitude of persons living under such conditions developed their own diseases.

There is an old saying that "virtue is its own reward." I think one could well say that cleanliness has a much greater reward in the way of health and longer life and happiness. It would seem that those who are engaged in making the world cleaner and destroying the causes of disease are engaged in a most important and responsible duty and should have the thanks and co-operation of all concerned and that is everyone.

SCIENTIFIC AND TECHNICAL ABSTRACTS

QUALITATIVE DETECTION OF MERCURY SENSITIVE TO ONE PART IN A BILLION.—Most of the qualitative tests previously used failed at a dilution greater than 5 mgms. of hg. per litre. A new method for the qualitative detection of hg. is described, which is sensitive to one part of mercury in two million parts of solution, and which by isothermal concentration at room temperature detects one part of hg. ion per billion. A 36-gauge (B. and S.) cu. wire is highly polished with emery paper to a fine point, and is cemented with de Khotinsky cement to a hollow ground glass slide in such a manner that the wire is firmly held with its free end sloping into the cavity. This serves as the cathode; a small pt. wire similarly mounted serves as an anode. These electrodes are connected to heavier wires, and then to a source of current. If a permanent apparatus is desired, small binding posts can be cemented to the glass slide about 2.5 cm. from the center of the cavity. These will keep the electrodes firmly in position, and also facilitate the removal of the cu. wires. A drop of the solution to be tested is placed in the cavity on the slide and acidified with

HNO_3. The pt. anode is set into the drop, but *only* the *tip* of the point of the cu. cathode is allowed to touch it. A current of 1.3-1.5 milliamperes and of 1.5-2 volts is then passed through the drop. When the solution is not extremely dilute, two to three minutes is long enough for detection of the hg. The circuit is then broken, the cu. wire is removed, washed with water and examined under the microscope. A silvery-white amalgam, turning greenish-yellow upon standing, shows the presence of hg. By this method the hg. in one drop of a solution of hg. salt containing 0.5 mgm. of hg. per litre can be detected; that is, a sensitivity of one part in two million. The sensitivity can be easily increased 1000-fold by evaporating 25-50 cc. of the test solution to a few drops in a vacuum desiccator over H_2SO_4. The residue is moistened with a drop of HNO_3, carefully stirred with a small, pointed glass rod to collect all the mercury salt into the drop, the drop then transferred to the glass slide and tested for hg. as described above. By using this preliminary concentration the electrolytic test is easily sensitive to one part one billion.—H. S. Booth and Nora E. Schreiber (*J. Amer. Chem. Soc.*, 1925, 47, 2625).

ECHITAMINE.—Alstonia scholaris and A. congensis have been examined by J. A. Goodson and T. A. Henry. The former has been found to contain two alkaloids, ditamine and echitamine. The various Alstonia barks are used in the localities where they occur, as remedies for malaria, but so far no attempt has been made to use echitamine in medicine. In experiments on mice echitamine hydrochloride has toxic effects producing paralysis of the medulla. The alkaloid is produced by exhausting the finely-ground bark with hot alcohol and pouring the warm concentrated solution into 1 per cent. acetic acid, extracted first with ether and then with chloroform, made alkaline with sodium hydroxide, and liberated with chloroform, dissolved in alcohol, and acidulated with 10 per cent. hydrochloric acid. The product from different samples of bark A. congensis varied considerably. Total alkaloids, per cent.—Gold Coast, 0.38 to 0.56; Nigeria, 0.11 to 0.12; Cameroons, 0.18. Echitamine hydrochloride—Gold Coast, 0.18 to 0.34; Nigeria, 0.03 to 0.04; Cameroons, 0.09. Echitamine occurs as hydrochloride, hydrioxide, sulphate, nitrate, neutral oxalate and picrate processes and determinations are given. —*Wellcome Chemical Research through Chem. and Druggist, Australia.*

NEW RAYS FILL UNKNOWN GAP.—Another gap in the spectrum of radiation, which includes light, X-rays, radio waves and the very short rays investigated by Millikan, has now been filled, it was announced today by Wynn Williams of the University of North Wales. He has been making investigations of sparking between electrodes and accidentally found the new rays, which are believed to fill part of the gap between the longer X-rays and the short ultra-violet rays, which lie beyond the violet in the visible spectrum. It is stated that the new rays will penetrate air for several meters and will go through thin celluloid films, but are stopped by solids such as gold leaf and even thin mica.—*Science Service.*

THE DETERMINATION OF COPPER IN FOODSTUFFS.—The colorimetric method of determining copper as ferrocyanide has been found more suitable than any of the other colorimetric methods tried. It is accurate to within about 5 per cent. A more exact method has been based on the fact that quinosol in neutral solution gives a quantitative precipitate with copper (Cu = 18.55 per cent.), in which one atom of copper appears to replace two atoms of hydrogen in the quinosol molecule. Metals precipitated by ammonia in excess do not give a precipitate with quinosol. The precipitated copper is determined by drying and weighing the precipitate or by an electrolytic method.—*L. H. Lampitt, D. Sc., F. I. C., E. B. Hughes, M. Sc., F. I. C., C. H. F. Fuller and P. Bilham.*

THE OCCURRENCE OF ARSENIC IN APPLES.—Attention was first directed to the recent outbreak of arsenical poisoning of apples, due to spraying with lead arsenate, as the result of two cases of illness. Only five out of thirty-nine samples of Jonathan, King David, and Newtown apples were found to be free from arsenic, and eleven contained more than the statutory limit. The contamination is mainly, but not entirely, confined to the skin, arsenic having been found in the flesh of the fruit to the extent of about 3 per cent. of that on the skin. Notwithstanding statements to the contrary, it appears that rain does not remove all the arsenic. Washing under the tap and even scrubbing was found to leave appreciable amounts of arsenic on the fruit, presumably owing to combination of the arsenic with the proteins of the skin.—*H. E. Cox, M. Sc., Ph. D., F. I. C.*

THE DIRECT TITRATION OF THALLOUS SALTS WITH POTASSIUM IODATE.—Thallous salts are quantitatively oxidized to the thallic condition by potassium iodate in presence of a sufficient concentration of hydrochloric acid. The iodine liberated is oxidized to iodine monochloride, the hydrolysis of which is prevented by the hydrochloric acid. The end-point is found by frequently shaking the liquid with chloroform, the violent color of the dissolved iodine disappearing when the reaction is complete. The presence of bromides does not interfere, the oxidization of the iodine being complete before any liberation of bromine occurs.—*A. J. Berry, M. A.*

THE DETERMINATION OF ASCARIDOLE IN CHENOPODIUM.—The usual methods of determining ascaridole by physical tests are liable to error owing to the presence of physiologically inactive products of ascaridole, and they may fail to detect certain adulterants. A method has been based on the reduction of ascaridole, which is an organic peroxide, by a standard solution of titanous chloride. Two samples of chenopodium oil thus examined contained 72 per cent. and 80 per cent. of ascaridole, whilst a third, which answered the requirements of the U. S. Pharmacopœia, contained only 48 per cent. and was found to be adulterated with cineol.—*H. Paget, B. A.—Soc. of Public Analysts* (*through Pharm. Journ.*)

ENGINE RUNS ON ATOMS—MINERAL SANDS CONTAINING TITANIUM HEATED TO 3100 DEGREES.—What may be described as the first practical patent for running an engine on power obtained from the atom has just been granted to a Dutchman.

He has discovered that if mineral sands containing titanium are heated to a temperature of 3100 degrees the atoms disintegrate, and an enormous amount of heat is generated.

The sand is heated in a small electric furnace, and the heat caused by the sudden breaking-up of the atom is forced by a pump through tubes that heat the water in a boiler, and supply the power to drive an engine or turbine.

This patent has passed through the Patent Office almost unnoticed, but it is actually the first stepping stone to the realization of the power from the atom which all the world is waiting for. It may easily develop into the most dramatic achievement of the century.

AROMATIC ESTERS OF ACYLECGONINES.—Naturally, occurring cocaine has served in several ways as a starting point in the search for the ideal local anæsthetic of low toxicity. The characteristics of its structure essential to the development of pronounced anæsthetic action are now recognized to the amino—and acylated alcohol groups (1). A large variety of aminoalkyl esters, not containing the bridged ring of cocaine, has been synthesized, and some of these, including novocaine, stovaine and B-eucaine, are in common use. In them, however, the power of penetrating mucous membrane possessed by cocaine, which, for example, renders it so valuable in causing corneal anæsthesia, is but feebly developed.

By replacing the methyl group of the formula by aromatic alcohol residues, Mr. Gray has produced substances which, on being tested in the Wellcome Physiological Research Laboratories by Dr. Trevan and Miss Boock, have given in the direction sought. Of the number all except three are more active anæsthetics than cocaine, as tested on the cornea of the rabbit. Five are better than cocaine when tested by subcutaneous injection, and of these two are active in one-eighth the concentration required by cocaine. In the case of two the toxicity on mice is only slightly greater than that of cocaine, but in the others it is considerably less. Further results are promised at a later date.—*W. H. Gray.* (*Wellcome Chemical Research through Chem. and Druggist, Australia*).

A NEW QUANTITIVE REAGENT.—Citarin, the sodium salt of a complex derivative of citric acid, was introduced in 1901 by the Elberfeld Company as a therapeutic agent. In 1917, Vanino reported in the *Kolloid-Zeitsch* (1917, *20,* 122) its use in colloid chemistry. Recently Vanino and Guyot have studied its application as a reagent for the determination of reducible metals. Their results, which as yet have been found satisfactory only with silver and gold, are reported in the *Ber. d. deut. Pharm. Gesell.* (1926, *36,* 98). When mixed with water, the salt undergoes hydrolysis with separation of formaldehyde and it was, therefore, inferred that reducible metals would be set free. Decinormal silver nitrate was mixed with citarin solution and sodium hydroxide of similar strength, heated for thirty minutes on the water-bath and allowed to stand overnight. The precipitate was collected on a suitable filter, washed and dried (at from 110 degrees to 120 degrees). A similar method was applied to gold chloride solution. The test analyses submitted show very satisfactory data. Experiments with bismuth have so far not yielded useful results. H. L.

KILLING GERMS WITH SOAP.—"Hot soap suds and water," the good old-fashioned remedy for all cleansing purposes, has real germicidal properties, according to experiments carried on at the Army and Navy General Hospital here by Dr. J. E. Walker.

In a forthcoming issue of the *Journal of Infectious Diseases,* Dr. Walker says that any ordinary soap used with a reasonable degree of care will kill several kinds of bacteria, notably those that cause pneumonia, gonorrhea, diphtheria and several of the pus-forming organisms. The dysentery and typhoid bacilli die harder. Strong soaps made of what is known as saturated fatty acids are necessary to annihilate these tough ones. A salt water soap, prepared exclusively from coconut oil, is the most readily available efficient soap to rid the hands of possible typhoid bacilli. Unfortunately, an all around coconut oil soap is too irritating to the skin for ordinary round use.—*Science Service.*

BOOK REVIEWS

MARVELS OF MODERN PHYSICS. G. P. Putnam's Sons, New York.

In the "Marvels of Modern Physics" this borderland which has to do with both physics and chemistry is thoroughly explored by Joseph McCabe, who brings to his task a keen appreciation of what is of interest, and a cleverness of interpretation which make the book attractive from the beginning of the first chapter to the end of the last. The chapter headings themselves speak for the scope of the book.

In the "Triumph of Science" is given a brief survey of the field to be covered. In "What Is Matter?" the atom, the molecule, and the element are discussed starting with Democratius, who was the originator of the atomic theory more than 2000 years before its confirmation and acceptance, and ending with the failure of Crookes to discover the electron when he dismissed the subject by calling a certain manifestation "radiant matter." The chapter on "The Wonderful Electron" will have an appeal and an interest to many who have become acquainted with that elusive factor in connection with "radio." Imagine measuring the speed and size of a particle that is 1850 times smaller than an atom, and the atom measures only 1-250,000,000 of an inch in diameter, which moves at the rate of speed of 150,000 to 170,000 miles a second, and which is never at rest. And yet this has been done, so often and with such accuracy that physicists have taken this as the unit or starting point for still more startling discov-

eries in connection with the structure of the atom. It will surprise many who have not read articles upon modern atomic structure or listened to lectures upon it, to learn for the first time that all matter, even including the densest metals, is composed of structural units called molecules, which are as discontinuous as the planets in our solar system; and that these molecules in turn are made up of atoms whose structure is likewise open.

Realizing the degree of compressibility to which substances would respond if we had the means of producing enough pressure, we can understand the meaning of a recent scientific news item to the effect that a star had been found by astronomers with a structure so dense that a volume of its content equivalent to one pint would weigh over thirty tons on our planet. A commodity with such a density would never need to be tied down or nailed fast to keep it from being casually picked up and carried away.

The Mysteries of Light, Wireless and other Waves, Electricity-Power Problems, The Transformation of Life, and a New View of the Universe are subjects discussed in a delightful style, and full of bewildering surprises for the reader who has not kept up with modern scientific theory. One thing that the book lacks to make it more valuable, is an index, for many users will wish to refer to certain statements which they will have difficulty in finding. For there are no synopses given under chapter headings.

CHARLES H. LAWALL.

POTTER'S COMPEND OF MATERIA MEDICA THERAPEUTICS AND PRESCRIPTION WRITING. 9th edition. By A. D. Bush, Professor of Pharmacology in Emory University. Price, $2.00.

The use of compends by students is a practice, we are happy to believe, much less frequent today than formerly. These books have a certain field of usefulness, for the purpose of refreshing the memory for State Board and similar examinations. To satisfactorily meet such a need a book must have its information concisely stated, well classified and accurate. Neither of the two latter requirements is well met by the present volume. The classification adopted appears to be based on no system, either pharmacologic, chemical or alphabetic. It brings such widely divergent substances as bismuth, quassia and eucalyptus into juxtaposition; it places such antagonistic drugs as veratrum and belladonna next to each other.

In the preface the author states that the present edition "has been thoroughly revised and brought into conformity with the 10th Revision of the U. S. Pharmacopœia." And again, "The whole work has been revised to conform with the best pharmacologic and therapeutic information." In the opinion of the reviewer neither of these statements is borne out by an examination of the text. For example: on page 3 appears the remarkable assertion that in the United States the pharmacopœia "has only the prestige of a professional publication," the author appears to be ignorant of the Food and Drugs Act of 1907, as well as the enactments of many state legislatures, giving the pharmacopœia the standing of a book of law. Of the new drugs added to the pharmacopœia, amidopyrine, calioben, carbromal, Rhus glabra and sodium biphosphate, are not described at all; albumin tannate and acetyl-tannic acid are listed under their proprietary names, but not under their official names; oil of chaulmoogra is mentioned only as a source of ethyl chaulmoograte; the only ointment of mercury referred to is the blue ointment, and the official name is not properly given, the strong ointment of mercury which is much more widely used in this country, is not mentioned at all.

We note the retention of such discarded chemical notions as that duboisine is a distinct alkaloid, that jalapin is a chemical individual, and that saponin is the name of a substance and not of a group of compounds.

The therapeutic statements are sometimes ultra modernistic and other times bear the stamp of ancient superstitions. For example, of creosote it is said that it "has been extensively used in phthisis, but today there is a wide healthful skepticism of its value"; on the other hand, he has faith to believe, apparently, that "globus hystericus may be often removed by ignatia," and that "stramonium is a good remedy" in chorea minor and stammering. He is familiar with the recent experiments of McGuigan which question the value of ferric hydroxid in arsenic poisoning, but still adheres to the long exploded theory that "any soluble sulphate" is a chemical antidote to phenol, and recommends the use of egg albumen in the treatment of poisoning by bichloride of mercury—which Fantus thoroughly demonstrated to be of practically no value—and he does not mention any of the modern antidotes to this deadly agent.

Taking all in all the book is not one we can conscientiously recommend.

H. C. Wood.